

IN THE SPECIFICATION:

Please replace paragraph [0003] with the following amended paragraph:

[0001] The present application claims the benefit of, and priority to U.S. Ser. No. 09/801,430, entitled "Parallel Gas Chromatograph with Microdetector Array" filed March 7, 2001, by Srinivasan et al., and U.S. Ser. No. 60/222,540 entitled "Parallel Gas Chromatograph with Microdetector Array" filed August 2, 2000 by Srinivasan et al., ~~which is~~ which are hereby incorporated by reference for all purposes.

Please replace paragraph [0003] with the following amended paragraph:

[0003] Gas chromatography, and in particular, multi-channel gas chromatography is known in the art. See, for example, PCT patent application ~~WO 00/23724~~ WO 00/23734 (Daniel Industries, Inc.). Thermal conductivity detectors are also known in the art, and have been routinely used for detection in gas chromatographs - alone, or in combination with other detectors. See, for example, U.S. Patent No. 4,594,879 to Maeda et al., and Great Britain Patent Specification GB 1,262,529.

Please replace paragraph [0004] with the following amended paragraph:

[0004] Combinatorial (i.e., high-throughput) catalysis is likewise known in the art. See U.S. Patent No. ~~4,985,356~~ 5,985,356 to Schultz et al., U.S. Patent No. 6,004,617 to

Schultz et al., U.S. Patent No. 6,030,917 to Weinberg et al., U.S. Patent No. 5,959,297 to Weinberg et al., U.S. Patent No. 6,063,633 to Willson, U.S. Patent No. 6,149,882 to Guan et al., and PCT applications WO 99/64160, WO 99/51980, WO 00/09255, WO 00/23921, WO 00/32308 and WO 00/51720 each of which patents and applications relates to various aspects of combinatorial materials science and combinatorial catalysis, and each of which (including corresponding US applications from which priority is claimed) is hereby incorporated by reference for all purposes.

Please replace paragraph [0008] with the following amended paragraph:

[0008] More specifically, the present invention is directed to a gas chromatograph having four or more analysis channels for simultaneous analysis of four or more fluid samples. The gas chromatograph comprises four or more gas chromatography columns (each comprising an inlet for receiving a gaseous mobile phase that includes a gaseous sample, a separation media effective for separating at least one separated component of the gaseous sample from other components thereof, and an outlet for discharging the separated gaseous sample) and a microdetector array comprising four or more thermal conductivity microdetectors for detecting the thermal conductivity of said at least one separated component of the gaseous sample, said thermal conductivity microdetectors being integral with a substrate or mounted on the substrate. The four or more thermal conductivity microdetectors generally have an inlet port in fluid communication with the outlet outlet of one or more of the gas chromatography columns for receiving a separated gaseous sample, a detection cavity, a thin-film

detection filament within the detection cavity for detecting at least one separated component of the separated gaseous sample, and an outlet port for discharging the separated gaseous sample.

Please replace paragraph [0009] with the following amended paragraph:

[0009] The gas chromatographs of the present invention include several variously characterized embodiments. The microdetectors are, in one embodiment, preferably microfabricated microdetectors that are integral with the substrate or with one or more microchip bodies mounted on the substrate. In another embodiment, the microdetectors are thermal conductivity detectors comprising a thin-film detection filament in the detection cavity, where the detection filament has a temperature-dependent resistance. In additional embodiments described in greater detail hereinafter, the microdetectors are bonded to the substrate, or are alternatively detachably mounted on the substrate, preferably as microchip bodies comprising one or more ~~microdetectors~~ microdetectors.

Please replace paragraph [0010] with the following amended paragraph:

[0010] In a particularly preferred embodiment, the gas chromatograph is a six-channel gas chromatograph for simultaneous analysis of six or more fluid samples. The gas chromatograph can comprise six or more gas chromatography columns (each of the six or more gas chromatography columns comprising an inlet for receiving a gaseous mobile phase that includes a gaseous sample, a separation media effective for

separating at least one separated component of the gaseous sample from other components thereof, and an outlet for discharging the mobile phase and the separated gaseous sample) and a microdetector array comprising six or more sample thermal conductivity ~~detectors~~ microdetectors and at least one reference thermal conductivity ~~detector~~ microdetector. Each of the sample and reference thermal conductivity ~~detectors~~ are microdetectors is integral with or mounted on a substrate with a planar density of at least about 1 thermal conductivity ~~detector~~ microdetector per 1 cm<sup>2</sup>, and the ratio of sample ~~detectors~~ thermal conductivity microdetectors to reference ~~detector(s)~~ thermal conductivity microdetector(s) is at least 2:1. Each of the six or more sample thermal conductivity ~~detectors~~ microdetectors comprises an inlet port in fluid communication with the outlet of one of the gas chromatography columns for receiving a separated gaseous sample, a detection cavity having a volume ranging from about 1 ml to about 500 ml for detecting at least one component of the separated gaseous sample, a thin-film detection filament within the detection cavity, the thin-film detection filament having a temperature-dependent resistance, an outlet port for discharging the gaseous sample, a first conductive path between the a first end of the thin-film detection filament and a first electrical contact, and a second conductive path between a second end of the thin-film detection filament and a second electrical contact. The first and second electrical contacts are adapted for electrical communication with one or more integral or external signal-processing circuits. The at least one reference thermal conductivity ~~detector~~ microdetector has an inlet port in fluid communication with a reference gas source for receiving a reference gas, a detection ~~cavity~~ comprising cavity, a thin-film detection filament within the detection cavity for detecting the

reference gas, and an outlet port for discharging the detected reference gas. The six or more sample thermal conductivity ~~detectors~~ microdetectors each have a thermal coefficient of resistance that varies less than about 10% between the six or more thermal conductivity ~~detectors~~ microdetectors.

Please replace paragraph [0012] with the following amended paragraph:

[0012] The invention is further directed to a microdetector array comprising four or more thermal conductivity ~~detectors~~ microdetectors. The four or more thermal conductivity ~~detectors~~ microdetectors are integral with or mounted on a substrate with a planar density of at least about 1 thermal conductivity ~~detector~~ microdetector per 10 cm<sup>2</sup>. Each of the thermal conductivity ~~detectors~~ comprise microdetectors comprises a detection cavity having a volume of not more than about 500  $\mu$ l, an inlet port for admitting a fluid sample into the detection cavity, one or more thin-film detection filaments within the detection cavity, the thin-film detection filament having a temperature-dependent resistance, an outlet port for discharging a fluid sample from the detection cavity, first and second electrical contacts for electrical communication with a signal-processing circuit, a first conductive path between the first electrical contact and a first end of the thin-film detection filament, and a second conductive path between the second electrical contact and a second end of the thin-film detection filament. In preferred embodiments, the microdetectors are mounted on the substrate, individually or as modules, by being bonded to the substrate, or by being detachably mounted on the substrate, in either case, preferably

as microchip bodies comprising one or more of the thermal conductivity microdetectors.

Please replace paragraph [0014] with the following amended paragraph:

[0014] The invention is also directed to a gas chromatograph, and methods of using the same, where the gas chromatograph has larger numbers of analysis channels - especially to systems having eight or more, and preferably sixteen or more, twenty-four or more, forty-eight or more or ninety-six or more gas chromatography columns adapted for simultaneous analysis of a like number of samples (e.g. such as are generated in a combinatorial catalysis experiment). Specifically, the gas chromatograph comprises eight or more gas chromatography columns residing in a heated environment, and a detector microdetector array comprising eight or more detectors thermal conductivity microdetectors (i.e. at least eight detection channels, whether in a single instrument, such as the preferred microdetector array described above, or in separate conventional detection instruments). Each of the of the eight or more gas chromatography columns have an inlet for receiving a gaseous mobile phase that includes a gaseous sample, a separation media effective for separating at least one separated component of the gaseous sample from other components thereof, and an outlet for discharging the separated gaseous sample. The heated environment is adapted to provide substantially the same temperature profile, temporally, for the eight or more gas chromatography columns - as measured at substantially the same spatial location on each column at a given time during a temperature excursion of at least about 10 °C. In particular,

the temperature of the eight or more columns is preferably substantially the same - as measured as such, and preferably does not vary by more than about 10 °C, preferably not more than about 5 °C, 2 °C, 1 °C, 0.5 °, and 0.1 °C, as measured as such. Additionally or alternatively, the heated environment provides a substantially uniform time-rate-of-change in temperature to each of the eight or more gas chromatography columns (e.g., during a temperature ramping excursion) - as measured at a given time during a temperature excursion at substantially the same spatial location of the compared columns. Preferably, the rate of change in temperature varies by not more than about 10%, and preferably not more than about 5 %, 2 %, 1 %, or 0.5 % as measured as such. In a particularly preferred embodiment, the heated environment comprises a forced convection zone for directed flow of a fluid in a substantially uniform direction past the eight or more gas chromatography columns. In any case, the eight or more detectors each have an inlet port in fluid communication with the outlet of one or more of the gas chromatography columns for receiving a separated sample, a detection cavity for detecting at least one component of the separated sample, and an outlet port for discharging the separated gaseous sample.

Please replace paragraph [0016] with the following amended paragraph:

[0016] The parallel detection systems of the present invention are of substantial importance for high-throughput combinatorial catalysis research programs. Parallel screening reactors, such as flow reactors as disclosed in U.S. Ser. No. 09/093,870 filed June 9, 1998 by Guan et al. (herein "98-13",

and now issued as U.S. Patent No. 6,149,882), U.S. Ser. No. 09/518,794 filed March 3, 2000 by Bergh et al. (herein "99-1"), U.S. Ser. No. 60/185,566 filed March 7, 2000 by Bergh et al. (herein "00-022"), U.S. Ser. No. [[\_\_\_\_\_]] 09/801,390, entitled "Parallel Flow Process Optimization Reactor Reactors" filed ~~on the date even herewith (March \_\_\_, 2001)~~ March 7, 2001, by Bergh et al., U.S. Serial No. [[\_\_\_\_\_]] 09/801,389, entitled "Parallel Flow Reactor Having Variable [[Feed]] Composition" filed ~~on the date even herewith (March \_\_\_, 2001)~~ March 8, 2001, by Bergh et al., and U.S. Serial No. [[\_\_\_\_\_]] 60/274,065, entitled "Parallel Flow Reactor Having Improved Thermal Control" filed ~~on the date even herewith (March \_\_\_, 2001)~~ March 7, 2001, by Bergh et al. can effect reactions in tens, hundreds or even thousands of channels simultaneously or substantially concurrently. Parallel detection systems, such as two-channel gas chromatography systems, have been advantageously applied in connection with some such parallel reaction systems, but are inherently limited by their size (bulk) and, significantly, by their cost per channel.

Please replace paragraph [0028] with the following amended paragraph:

[0028] FIG. 8A and 8B 8A through 8K are schematic diagrams for the electrical circuitry associated with the parallel thermal conductivity microdetectors of the invention.

Please replace paragraph [0035] with the following amended paragraph:

[0035] The present application is related to the following U.S. patent applications, each of which is hereby incorporated by reference for all purposes: US Ser. No. 09/093,870 filed June 9, 1998 by Guan et al. (herein "98-13"), now issued as U.S. Patent No. 6,149,882; US Ser. No. 09/518,794 filed March 3, 2000 by Bergh et al. (herein "99-1"); US Ser. No. 60/185,566 filed March 7, 2000 by Bergh et al. (herein "00-022"); U.S. Ser. No. [[\_\_\_\_\_]] 09/801,390, entitled "Parallel Flow Process Optimization Reactor Reactors" filed ~~on the date even herewith (March \_\_\_\_\_, 2001)~~ March 7, 2001, by Bergh et al.; U.S. Serial No. [[\_\_\_\_\_]] 09/801,389, entitled "Parallel Flow Reactor Having Variable [[Feed]] Composition" filed ~~on the date even herewith (March \_\_\_\_\_, 2001)~~ March 8, 2001, by Bergh et al.; and U.S. Serial No. [[\_\_\_\_\_]] 60/274,065, entitled "Parallel Flow Reactor Having Improved Thermal Control" filed ~~on the date even herewith (March \_\_\_\_\_, 2001)~~ March 7, 2001, by Bergh et al.; U.S. Serial No. [[\_\_\_\_\_]] 60/274,022 entitled "Microvalve Arrays for Gas Chromatograph Injection" filed ~~on the date even herewith (March \_\_\_\_\_, 2001)~~ March 7, 2001, by Bergh et al.; US Ser. No. 09/285,363 filed April 2, 1999 by Petro et al. (herein "99-9"); US Ser. No. 09/174,856 filed October 19, 1998 by Lacy et al. (herein "98-11"); US Ser. No. 09/156,827 filed September 18, 1998 by Giaquinta et al. (herein "99-21"); and US Ser. No. 09/516,669 filed March 1, 2000 by Lugmair et al. (herein "99-66").

Please replace paragraph [0043] with the following amended paragraph:

[0043] The microdetector array 500 generally comprises four or more detectors 510 integral with, or alternatively, mounted on a substrate 600. The four or more microdetectors 510 are generally flow detectors, and comprise an inlet port in fluid communication with the ~~outlet~~ outlet of one or more of the gas chromatography columns for receiving a separated sample, a detection cavity for detecting at least one component of the separated sample, and an outlet port for discharging the sample. The microdetectors can be any type of detector suitable for gas chromatography detection. Preferred detectors include those selected from the group consisting of thermal conductivity detectors, photoionization detectors, optical emission detectors, flame ionization detectors, surface acoustic wave detectors and pulse discharge detectors. Thermal conductivity detectors are particularly preferred in connection with the present invention (including in particular, with this embodiment of the invention), for many applications, in view of their universality (with respect to capabilities for analyzing various types of samples) and sensitivity (with respect to capabilities to detect low concentrations of analyte). Thermal conductivity detectors are advantageous, for example, with respect to relative simplicity of the electronics, a lack of hysteresis concerns, etc. Other types of detectors may, however, be advantageously applied for particular applications of interest. For each types of detectors, the detectors may further comprise other components, as appropriate, including for example, a detection filament having a temperature-dependent resistance for thermal conductivity detectors, or as another example, windows transparent to electromagnetic energy of particular wavelengths of interest (e.g. an optically-transparent window) for detector types requiring application of such electromagnetic energy.

Although the invention is described in further detail herein primarily in connection with thermal conductivity detectors, the invention is not limited to such detectors unless specifically recited in the claims. A person of skill in the art can adapt the concepts disclosed herein for applications to other types of detectors.

Please replace paragraph [0045] with the following amended paragraph:

[0045] In another embodiment, the microdetector array comprises four or more thermal conductivity detectors integral with or mounted on a substrate, each comprising one or more thin-film detection filaments. Specifically, with reference to Figure 5A, each of the four or more thermal conductivity microdetectors 510 in this embodiment comprises an inlet port 512 in fluid communication with the ~~outlet~~ outlet of one or more of the gas chromatography columns for receiving a separated sample, a detection cavity 516 comprising at least one thin-film detection filament 520 within the detection cavity 516 for detecting at least one component of the separated sample, and an outlet port 514 for discharging the sample from the detection cavity 516. As discussed below, the particular design of the thermal conductivity detector is not narrowly critical, and can include known or later-developed designs.

Please replace paragraph [0079] with the following amended paragraph:

[0079] In operation, the TCD's are typically operated in a constant voltage mode, but may also be operated in a constant

power mode or other modes that those of skill in the art will recognize based on this disclosure. For example, Figures 8A and 8B 8A through 8K present detailed schematics of the electronics for the electrical measurement circuitry - that is, of the signal processing circuit(s) - for a six channel embodiment. As illustrated, the six TCD's 510 form the top half of a Wheatstone bridge with a common reference TCD 511 (Figure 8A). Each leg of the bridge has external potentiometers for bridge balancing. The bridge output is amplified using an instrumentation amplifier and filtered before being sent to a data acquisition board. The electronics are mounted on a single printed circuit board, the schematic of which is shown in Figure 8B. External DC power is applied to Connector 3 (CON3). The bridge voltage is adjusted using a potentiometer. Pogo pins may connect the nine TCD's to the electronics board (Connector 10, CON10), although other embodiments may be used. Each TCD typically has two potentiometers for coarse and fine nulling of the bridge. Switches are used to select six out of the nine TCD's for measurement and to pick the reference TCD. Alternate modes of operation include a constant temperature mode and a constant power mode, both of which require modifications to the electronics, but that those of skill in the art will be able to practice upon review of this specification.

Please replace paragraph [0092] with the following amended paragraph:

[0092] For gaseous samples, and especially gaseous samples to be analyzed directly from a parallel flow reactor, such as a parallel flow process optimization reactor (discussed below), the parallel injection valve is preferably a multi-

channel valve where each channel achieves injection into one of the channels gas chromatography column by an array of microvalves, preferably membrane-actuated microvalves. A particularly preferred injection valve for such applications is disclosed in co-pending U.S. Serial No. [[\_\_\_\_\_]] 60/274,022 entitled "Gas Chromatograph Injection Valve Having Microvalve Array" filed ~~on the date even herewith (March 7, 2001)~~ March 7, 2001, by Bergh et al.

Please replace paragraph [0095] with the following amended paragraph:

[0095] The parallel reactor can be of any type known in the art. Preferably, the reactor can be a parallel batch reactor, a parallel semicontinuous reactor, or a parallel flow reactor. A parallel flow reactor preferably comprises four or more reaction vessels, each of the four or more reaction vessels comprising an inlet for feeding reactants into the reaction vessel, a reaction zone for effecting a chemical reaction, and an outlet for discharging reaction products and unreacted reactants, if any, the outlets of the four or more reaction vessels being in at least sampling fluid communication with the inlets of the four or more gas chromatography columns, respectively. For investigating catalyst composition in a heterogeneous catalysis system, a parallel flow reactor such as described in U.S. Patent No. 6,149,882 to Guan et al. (parallel fixed bed reactor), or as described in PCT application WO 00/51720 by Bergh et al. (massively parallel microreactor) are particularly preferred, and are hereby incorporated by reference. For investigating process conditions (including optimization of reaction conditions) in a heterogeneous

catalysis system, a parallel flow reactor such as described in the following co-pending patent applications are particularly preferred, and are hereby incorporated by reference: U.S. Ser. No. [[                ]] 09/801,390, entitled "Parallel Flow Process Optimization Reactors" filed ~~on the date even herewith (March 7, 2001)~~ March 7, 2001, by Bergh et al.; U.S. Serial No. [[                ]] 09/801,389, entitled "Parallel Flow Reactor Having Variable [[Feed]] Composition" filed ~~on the date even herewith (March 7, 2001)~~ March 8, 2001, by Bergh et al.; and U.S. Serial No. [[                ]] 60/274,065, entitled "Parallel Flow Reactor Having Improved Thermal Control" filed ~~on the date even herewith (March 7, 2001)~~ by Bergh et al.. March 7, 2001, by Bergh et al.